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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,628	02/27/2004	Ralph M. Ellison	CP380H	7657

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EXAMINER	
PAK, JOHN D	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 07/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/789,628	ELLISON ET AL.	
	Examiner	Art Unit	
	JOHN PAK	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *14-17 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13, 18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-20 are pending in this application.

Applicant is requested to update the continuity data in the specification by including the patented status of the parent application.

Applicant's election with traverse of the invention of Group II (claim 18) in the response filed on 4/24/2006 is acknowledged. Applicant argues that a separate and divergent search would not be required because a generalized search of the subject matter of any one of the invention groups would necessarily lead to disclosures encompassed by the other invention groups. Applicant further states that similar classification of the inventions shows that search and examination of the entire application would not impose a serious burden on the Examiner. The Examiner cannot agree.

First, applicant's statements are inconsistent with applicant's own prior actions. Applicant has claimed the following in four separately filed patent applications:

Application No.	**Claimed subject matter**
10/640,399	Treatment of multiple myeloma with arsenic
10/649,944	Treatment of lymphoma with arsenic
10/649,776	Treatment of melanoma with arsenic
10/640,403	Treatment of myeloid dysplastic syndrome with arsenic

Such separately filed applications are evidence of recognition in the art of separate patentability and multiple subjects of inventive effort for treatment of various cancer types with arsenic.

Second, the U.S. Patent Classification system is not always indicative of the divergent searches and complex technology-specific considerations that would be required. This is particularly the case in complex technologies where the classification system has not kept up with the developments in the art. For example, applicant argued during the prosecution of 10/649,776 that even a prior art reference that explicitly discloses "body surface tumors" and "skin cancer" is distinguishable over a claim directed to melanoma because there are many different types of skin cancers, such as basal cell carcinoma, squamous cell carcinoma, cutaneous T-cell lymphomas, Kaposi's sarcoma (reply filed on 3/7/2006). Applicant argued that different approaches are taken towards treating different types of skin cancer and the prior art disclosure of "body surface tumors" and "skin cancer" fails to provide reasonable expectation of success for treating melanoma. Clearly, applicant's arguments there are in contradiction of applicant's argument in this application. The same inventors clearly recognized separate technology-specific considerations and separate prior art analyses even among different types of skin cancers.

Third, applicant argues that the search and examination of the three invention groups would not impose a serious burden on the Examiner. The Examiner cannot

agree. As shown above, the examination of this application may turn on the preciseness of prior art teachings and technology-specific issues, and the burden represented by having to separately search AND separately consider the various different types of cancers to be treated vis-a-vis the prior art would place an undue burden on the Examiner. Undue burden is a relative and balanced concept since if the Examiner were given several weeks of time to search and examine this application, the burden would decrease. Applicant should keep in mind that this Examiner is given less than 14 hours to complete this case, from start to finish (allowance, abandonment or Examiner's Answer). Undue burden is also in plain view just from applicant's numerous information disclosure statements filed in the parent application (but not yet here): at least 7 pages worth of prior art listing were submitted. With so much relevant prior art and so many different types of cancers to consider, the specifics of this application support the Examiner's previous determination of undue burden.

Applicant's traversal of the outstanding restriction requirement is therefore found unpersuasive and the restriction requirement of record is thereby made FINAL.

Examination of this application shall be limited to the elected subject matter. Claims 1-13, 18 and 20 will presently be examined *to the extent* that they read on the elected subject matter. Claims 14-17 and 19 are withdrawn from further consideration as being directed to non-elected inventions.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-13, 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Zhang (US 6,720,011) and Sacchi et al. in view of CN 1121807 and Shimotsuura et al.

Zhang discloses treating lymphoma with arsenic trioxide. See column 1, lines 34-35 and 41-43. Intravenous composition containing 1-10 g arsenic trioxide, sodium chloride and water (column 1, lines 41-54). "[S]trong abruptive effect on the membranes of cancer cells" is disclosed, as well as inhibition of DNA/RNA synthesis (column 1, lines 58-61). Effective daily dose for an adult is disclosed as 10 ml of the composition containing 10 g/l arsenic trioxide added to 500 ml of 10% glucose solution is disclosed. This calculates to about 67 mg/day. Appropriate dose is to be "decreased accordingly for children" (column 2, lines 9-16).

Sacchi et al. teach all-trans retinoic acid (ATRA) in the treatment of various hematological malignancies such as several types of lymphomas (bottom of page 114, right column to top of page 115, left column).

CN 1121807 discloses administering arsenic trioxide as an injection to treat lymphatic cancer (page 4 of the English translation, last paragraph). The formulation of arsenic trioxide is referred to as Ai Ling (see pages 5-6 of the English translation, in particular page 6, last paragraph). Inhibition of DNA/RNA synthesis is disclosed (page 5 of the English translation, lines 6-7).

Shimotsuura et al. disclose that antineoplasmic actions of arsenic trioxide are primarily achieved by DNA composition blockage (page 25 of the English translation, top of page 49 in the original).

Zhang does not explicitly disclose treating lymphoma in a human by administering arsenic in combination with ATRA, optionally with other therapeutic agent(s). However, for the reasons to follow, the claimed invention as a whole would nonetheless have been obvious to the ordinary skilled artisan in this field at the time the invention was made.

Zhang is clear in that arsenic trioxide is effective against "lymphoma." There is no limitation as to the type of lymphoma. Lymphoma is typically a Hodgkin's lymphoma or non-Hodgkin's lymphoma, so inclusion of both would have been obvious to the ordinary skilled artisan. Further, Zhang teaches a strong abruptive effect on the membranes of cancer cells and inhibition of DNA/RNA synthesis. Taken with teachings of Shimotsuura et al., which confirm the DNA composition blockage action of arsenic trioxide antineoplastic activity and teachings of CN 1121807, which expand on Zhang's

teaching of efficacy against lymphoma by teaching efficacy against the broader "lymphatic cancer," the ordinary skilled artisan in this field would have been motivated to administer arsenic trioxide to treat patients with the specific lymphomas recited in the instant claims.

Ionic aqueous solution (applicant's claim 3) is met by the sodium chloride present in the arsenic trioxide solution (Zhang's column 1, lines 44-45). Varying the dose according to the body weight of a human (applicant's claim 12) is met by Zhang's explicit disclosure to decrease the dose for children. The claims are thereby rejected.

As for combined use with ATRA and radiation or other chemotherapeutic agents, such method would have been fairly suggested from the conventional practice in the cancer treatment field to combine the actions and benefits of several therapies to attack the cancer cells from a variety of mechanisms. ATRA is already known to have activity against lymphomas and the therapeutic agents listed in claim 11 are all well-known anti-cancer agents; hence, inclusion of such additional anti-cancer agents in combination with arsenic trioxide and ATRA would have been fairly suggested.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly suggested by the teachings of the cited references.

Claims 1-13, 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Zhang (US 6,720,011) and Sacchi et al. in view of CN 1121807, Li et al. and Shimotsuura et al.

Zhang, Sacchi et al., CN 1121807 and Shimotsuura et al. are relied on for the same teachings as in the preceding ground of rejection. Discussion of their teachings there is incorporated herein by reference.

Li et al.[1] disclose treating 27 patients with malignant lymphoma, including Hodgkin's disease, with Ailin-1 (see the English translation on page 62). 70.37% remission rate reported (id.).

Li et al. add to the previous discussion of the prior art in that they provide clinical report of 70.37% remission after treating 27 patients with malignant lymphoma, including Hodgkin's disease. The transliteration of Li's chemo-therapeutic formulation is "Ailin-1." From CN 1121807, it is known that "Ai Ling" formulations contain arsenic trioxide. It is the Examiner's position that the ordinary skilled person in the art of treating lymphatic cancers (including those artisans in the U.S. and China) would have recognized various transliterations such as "Ailin-1" and "Ai Ling" to be the same or similar Chinese formulations, which all contain arsenic trioxide.

Hence, Li et al. add to the previously discussed body of knowledge concerning arsenic trioxide and lymphatic cancer efficacy by specifically teaching efficacy against

malignant lymphoma, including Hodgkin's disease. In sum, Zhang teaches a strong abruptive effect on the membranes of cancer cells and inhibition of DNA/RNA synthesis. Taken with teachings of Shimotsuura et al., which confirm the DNA composition blockage action of arsenic trioxide antineoplastic activity and teachings of CN 1121807, which expand on Zhang's teaching of efficacy against lymphoma by teaching efficacy against the broader "lymphatic cancer," the ordinary skilled artisan in this field would have been motivated to administer arsenic trioxide to treat patients with the specific lymphomas recited in the instant claims, particularly in view of Li et al. Additionally, since all of the lymphomas recited in applicant's claims are cancers of the lymphatic system with uncontrolled growth of cells of similar functions and origin, one having ordinary skill in the art would have been motivated to administer arsenic trioxide to treat such lymphomas, particularly in view of its adverse effect on rapid DNA replication.

As for combined use with ATRA and radiation or other chemotherapeutic agents, such method would have been fairly suggested from the conventional practice in the cancer treatment field to combine the actions and benefits of several therapies to attack the cancer cells from a variety of mechanisms. The therapeutic agents listed in claim 11 are all well-known anti-cancer agents and inclusion of such additional anti-cancer agents in combination with arsenic trioxide and ATRA would have been fairly suggested.

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[1] Chinese J. Oncology, Vol. 10, pages 61-62 (1988).

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly suggested by the teachings of the cited references.

Claims 1-13, 18 and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-11, 13-17 and 19-20 of copending Application No. 10/649,944 in view of Sacchi et al.. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

Copending application claims 9-10 require arsenic trioxide to be combined with *at least* one other chemotherapeutic or radiotherapeutic agent, and claim 11, which depends on claim 9, encompasses ATRA as one such additional therapeutic agent. Thus, the copending claims encompass the same subject matter when ATRA is selected as one of the 19 specific additional therapeutic agents set forth in copending claim 11. Such selection of ATRA as one of the "at least one other therapeutic agent" is not only suggested by the copending claimed invention but also by Sacchi et al., who teach all-trans retinoic acid (ATRA) in the treatment of various hematological malignancies such as several types of lymphomas (bottom of page 114, right column to top of page 115, left column).

Therefore, the ordinary skilled artisan in this field would have recognized the instant invention to be an obvious variation of the invention set forth in the copending application claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

For these reasons, all claims must be rejected.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to JOHN PAK whose telephone number is **(571)272-0620.** The Examiner can normally be reached on Monday to Friday from 8 AM to 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's SPE, Johann Richter, can be reached on **(571)272-0646**.

The fax phone number for the organization where this application or proceeding is assigned is **(571)273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN PAK
PRIMARY EXAMINER
GROUP 1200